REMARKS

Claims 1 and 3 have been amended to incorporate the limitations of claim 17 and part of claim 50. Claims 1, 2, and 4 have been amended to correct minor typographical errors. Claim 10 has been withdrawn as drawn to a non-elected invention. Claims 12 and 17 have been canceled.

No new matter has been added.

Restriction

The Examiner commented on which aspects of the claimed invention are withdrawn from prosecution, in particular portions of the invention claimed in claim 4, 44 and 47, and the decapeptide of claim 51 (page 2-3 of the Office Action). Applicant respectfully requests reconsideration.

Certain embodiments of claims 4, 44, and 47 were indicated by the Examiner to be withdrawn. Applicant respectfully requests examination of these additional species upon a finding of allowable claims directed to the species wherein the amino acid adjacent to the N-terminal amino acid is L and the C-terminal amino acid is L.

Claim 51 recites a decapeptide that comprises the nonapeptide claimed in claim 44. The Examiner asserts that a decapeptide is structurally and functionally distinct from a nonapeptide. While Applicant can agree that a decapeptide may possibly be structurally and even functionally distinct from a nonapeptide, in this case the dependence from claim 44 requires both structural and functional similarity with the claimed nonapeptide. Claim 44 requires that the nonapeptide has certain sequence features; these sequence features also are required to be part of the decapeptide of claim 51. Similarly, claim 1 (from which claim 44 depends) requires that a peptide complexes with a major histocompatibility complex molecule type HLA-A2. Thus, the

structural and functional features of the nonapeptide and decapeptide are shared. Therefore, the decapeptide should be examined together with the nonapeptide.

Claim Objections

The Examiner objected to claims 1, 2, 17, 44-50 and 52-54 because claims 1, 2 and 17 contain periods that are not at the end of the claim. These periods were part of the expression "SEQ.ID.NO.", which has been corrected to recite "SEQ ID NO:". Withdrawal of the objection is respectfully requested.

The Examiner objected to claim 12 as not further limiting claim 11. Applicant has canceled claim 12 and respectfully requests withdrawal of the objection as moot.

Rejection Under 35 U.S.C. 112, First Paragraph

Written Description

A The Examiner rejected claims 1, 2, 11, 12, 17, 44-50 and 52-54 as lacking an adequate written description. Applicant respectfully traverses the rejection.

In part A of the rejection, the Examiner stated that "due to the open language 'comprising' [the claims] encompass unknown sequences attached to a fragment of SEQ ID NO:1."

Applicant respectfully disagrees with the Examiner's conclusion for the following reasons. Applicant provided in the specification the sequence of SEQ ID NO:1 as well as specific subsequences thereof. Other sequences that could be joined to these sequences are either known to the person of skill in the art using them or are known in the prior art. This type of disclosure has been deemed sufficient to provide an adequate written description by the CAFC

in the case of Capon v. Eshhar v. Dudas 418 F.3d 1349 (Fed. Cir. 2005). In that case, known polypeptides were combined to create a new chimeric protein, which the court found to be adequately described.

The court concluded that with respect to the sequences present in the claimed invention

> "... the law must take cognizance of the scientific facts. The Board erred in refusing to consider the state of the scientific knowledge, as explained by both parties, and in declining to consider the separate scope of each of the claims. None of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., Regents v. Lilly, Fiers v. Revel, Amgen, or Enzo Biochem, require a re-description of what was already known." Capon at 1357.

The court continued:

> "The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result." Capon at 1358.

The court concluded that:

> "In summary, the Board erred in ruling that §112 imposes a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field." Capon at 1360.

Thus, in view of the law as enunciated by the CAFC in Capon v. Eshhar v. Dudas, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1, 2, 11, 12, 17, 44-50 and 52-54 as lacking an adequate written description.

Moreover, according to Vas-Cath v. Mahurkar, 35 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991), the specification must "clearly allow person of ordinary skill in the art to recognize

that [he or she] invented what is claimed." Based on the knowledge of the skilled person as described above, the skilled person would readily recognize that Applicant invented the claimed invention.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 2, 11, 12, 17, 44-50 and 52-54 as lacking an adequate written description.

B. The Examiner rejected claims 2, 47-49 and 52-54 as lacking an adequate written description. Applicant respectfully traverses the rejection.

In part B of the rejection, the Examiner stated that Applicant "has not identified which amino acid fragments are critical or essential characteristics of the claimed linear and conformational B and T cell epitopes other than the linear peptides of SEQ ID NO:42 and 44". Applicant respectfully disagrees with this statement.

First, Applicant is not claiming the invention as broadly as implied by the Examiner's statement. Applicant specifically claims parts of SEQ ID NO:1 that form complexes with HLA-A2, particularly HLA-A2.1. Applicant disclosed in the application that a well-known method described by Rammensee et al. (see Example 3) for determining peptides was used to identify HLA-A2 binding peptides, which were then synthesized and tested for the ability to form complexes. As these methods are well known in the art, the skilled person would readily understand that Applicant was in possession of, and therefore had invented, that which is now claimed.

This disclosure also demonstrates that another of the Examiner's assertions, that "there is no known common structure of the claimed genus", also is incorrect. Applicant described that the peptide binding motif was a nonapeptide or decapeptide having Leu or Met at position 2 and Leu, Val or Ile at the carboxyl terminus, in accordance with the teachings of Rammensee et al. Thus, there quite clearly is a common structure in the claimed polypeptides, and this would be clear to the skilled person based on Applicant's disclosure.

The combination of (1) the requirement that the claimed peptide complexes with HLA-A2, the recognition sequence of which is known in the art as evidenced by Rammensee, and (2) the requirement that the peptide is a subsequence of SEQ ID NO:1, provides an amply detailed description of the claimed invention. In fact, the description provides a genus of peptides that can be immediately identified as part of the invention by the skilled person.

As indicated by the Examiner, the Enzo case provides that a partial structure and functional characteristics coupled with a known or disclosed correlation between function and structure are adequate to satisfy the written description requirement of 35 U.S.C 112, first paragraph. Enzo Biochem, Inc. v. Gen-Probe, Inc. 296 F.3d 1316, 63 USPA2d 1609 (Fed. Cir. 2002). Applicant has provided exactly that: the sequence of SEQ ID NO:1 (MAGE-A10) and the HLA-A2 recognition sequence, which couples function (complexing with HLA-A2) with structure (amino acid sequence binding motif). Thus, contrary to the Examiner's assertions, the standards for written description as enunciated by the courts have been satisfied.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 2, 47-49 and 52-54 as lacking an adequate written description.

Enablement

1. The Examiner rejected claims 1, 2, 4, 5, 9, 11, 12, 17, 42-50 and 52-54 as not enabled by the specification. Applicant respectfully traverses the rejection.

The Examiner's basis for rejecting the claims as lacking enablement is that "[o]ne cannot predict that a polypeptide comprising a fragment or a nonapeptide of SEQ ID NO:1, or the nonapeptide SEQ ID NO:42 could be used for producing antibodies or CTLs effective for diagnosis or treatment of diseases associated with SEQ ID NO:1, and especially cancer, because one cannot predict that the polypeptide SEQ ID NO:1 is expressed in an adequate amount on primary cancer cell surface, or cells from tissues with diseases." (Office Action at page 16).

Applicant respectfully disagrees with the Examiner's reasoning for at least the following reasons: the specification provides more than sufficient guidance for the skilled person, and nature of the invention and the level of skill in the art is such that the skilled person would not be required to conduct anything other than routine experimentation to practice the claimed invention.

The experimental examples in the specification describe the identification of antigenic peptides from MAGE-A10 and their ability to stimulate lysis of tumor cells expressing MAGE-A10 by cytotoxic T lymphocytes (Examples 1-3). Example 5 shows that allogeneic tumors cells that express MAGE-A10 were able to stimulate CTLs. Therefore, Applicant's specification contains working examples that demonstrate that MAGE-A10 is expressed and processed appropriately to permit recognition by T cell receptors (as shown by stimulation of CTLs). Therefore, one of ordinary skill in the art would have a reasonable expectation of success in using a polypeptide comprising a fragment or a nonapeptide of SEQ ID NO:1, or the nonapeptide SEQ ID NO:42, for producing antibodies or CTLs effective for diagnosis or treatment of diseases associated with SEQ ID NO:1.

Applicant also notes that, contrary to the Examiner's apparent requirement for "predicting" that a polypeptide in the manner described above, the enablement requirement provides that the skilled person not have to use undue experimentation in practicing the claimed invention. As is asserted above, Applicant's specification provides working examples and guidance that is sufficient such that the skilled person need only routine experimentation to practice the claimed invention. This is particularly true in view of the high level of skill in the art as is reflected in the level of knowledge in the scientific and patent literature. Numerous examples of antigenic tumor peptides (termed "tumor rejection antigens") in the literature and their use are provided in the specification on pages 1-3.

Thus the person of ordinary skill in the art has a high level of skill in the field of the claimed invention. When combined with the general guidance and specific working examples in Applicant's specification, it is clear that the skilled person would not have to exercise undue

experimentation to practice the claimed invention. Any experimentation that may be needed would be entirely routine in the art.

Furthermore, Applicant notes that the claimed invention is directed to isolated polypeptides that have uses other than the use singled out by the Examiner. Preparation of the claimed polypeptides, given the sequences and experimental guidance provided in the specification, would not require undue experimentation by the skilled person. Indeed, such preparation is entirely routine in the art, as evidenced by the long history of tumor rejection antigen peptides that is mentioned in the background section of the specification on pages 1-3.

Accordingly, Applicant respectfully request that the Examiner withdraw the rejection of the claims as not enabled.

2. The Examiner also rejected claims 4, 5, 11, 12, 42 and 43 as not enabled "because one cannot predict that the claimed nonapeptide could bind to HLA-A2 molecule and elicits a CTL response useful for diagnosis or treatment of diseases, especially cancer. (Office Action, page 22). Applicant has canceled claim 12. Applicant respectfully traverses the rejection with respect to the other named claims.

To ensure correctness of the record, Applicant notes that the Examiner's statement that "the nonapeptide of claim 4 encompasses the sequence XLXXXXXXL, wherein the amino acid at position 1, 3-8 could be any amino acid" (Office Action at page 22) is clearly incorrect. Claim 4 recites a nonapeptide comprising an unbroken sequence of amino acids from SEQ ID NO:1 wherein the amino acid adjacent to the N-terminal amino acid is L or M, and the C-terminal amino acid is L, V, or I. SEQ ID NO:1 is the amino acid sequence of MAGE-A10 protein. Therefore, there are a finite number of nonapeptides claimed in the claims rejected by the Examiner. Moreover, claim 4 excludes from the claimed subject matter a nonapeptide having the sequence CLGLSYDGL. Therefore, the "X" amino acids clearly cannot be any amino acid as asserted by the Examiner.

Regarding the rejection, Applicant notes that the claims are not diagnostic method or treatment method claims. Therefore, the Examiner's rejection of the claims as not enabled is not well founded.

Nevertheless, as already described earlier in this paper, the guidance in Applicant's specification, the working examples, and high level of skill in the art are such that the skilled person clearly would not have to exert undue experimentation to practice the claimed invention. Specifically, the specification teaches the person of skill in the art which nonapeptides are claimed, and provides the full sequence of MAGE-A10. It therefore is a trivial exercise for the skilled person to identify the claimed compositions, and to make them. Thus the person of skill in the art can make and/or use the claimed invention without undue experimentation, as is required for the claims to be enabled.

3. The Examiner further rejected claims 1, 2, 11, 12, 17, 44-50 and 52-54 as not enabled because " one cannot predict that the unbroken sequence of SEQ ID NO:1 or the nonapeptide would be exposed on the surface of the claimed sequence comprising said unbroken sequence or nonapeptide, in view of the teaching of Bowie et al." (Office Action at page 24). Applicant respectfully traverses the rejection.

Applicant maintains that the claimed invention is fully enabled in view of the guidance in Applicant's specification, the working examples, and high level of skill in the art. In particular, the working examples in the specification demonstrate that CTLs recognize MAGE-A10 peptides presented by cells. Example 5, in fact, demonstrates that allogeneic cells present MAGE-A10 peptides recognized by CTLs. Therefore, the specification provides more than adequate guidance to allow the skilled person to practice the claimed invention without the use of undue experimentation.

Rejection Under 35 U.S.C. 102(e)

1. The Examiner rejected claims 1, 2, 17, 44-50 and 52-54 as anticipated by US 5,912,143. Applicant respectfully requests reconsideration of the rejection.

Applicant has amended claims 1 and 2 to include the limitation of claim 17 that the claimed polypeptide is not that set out in SEQ ID NOs:1 or 2, or that coded for by nucleotides 334-918 of SEQ ID NO:7. Since the amino acid sequence of the prior art is 100% similar to SEQ ID NO:1, the amendment clearly eliminates the prior art from the scope of the claim. Therefore, the cited reference does not anticipate the claimed invention.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 2, 17, 44-50 and 52-54 as anticipated by US 5,912,143.

2. The Examiner rejected claims 1, 4, 11-12, 17 and 42-46 as anticipated by US 6,682,731. Applicant respectfully requests reconsideration of the rejection.

The Examiner asserted that SEQ ID NO:20 of US 6,682,731 is the same as a nonapeptide fragment of claim 1. SEQ ID NO:20 of US 6,682,731 is Gly Leu Glu Gly Ala Gln Ala Pro Leu (GLEGAQAPL), which also was identified in the present application as SEQ ID NO:50. Applicant has amended the claims to exclude this peptide, based on the limitation present in claim 50. Therefore, the amendment clearly eliminates the prior art from the scope of the claim and thus the cited reference does not anticipate the claimed invention.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 4, 11-12, 17 and 42-46 as anticipated by US 5,912,143.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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